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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/583,674

07/31/2006

Anne Boulay

33564-US-PCT

4528

1095

7590

11/13/2007

NOVARTIS

CORPORATE INTELLECTUAL PROPERTY

ONE HEALTH PLAZA 104/3

EAST HANOVER, NJ 07936-1080

EXAMINER

NATARAJAN, MEERA

ART UNIT

PAPER NUMBER

1643

MAIL DATE

DELIVERY MODE

11/13/2007

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/583,674	<b>Applicant(s)</b> BOULAY ET AL.	
	<b>Examiner</b> Meera Natarajan	<b>Art Unit</b> 1643	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 05 October 2007.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 5-10 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 5-10 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)  | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date <u>06/19/2006</u> . | 6) <input type="checkbox"/> Other: _____  |

**DETAILED ACTION**

***Election/Restrictions***

1. Applicant's election of Group 1, claims 5-10 in the reply filed on 10/05/2007 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).
2. Claims 5-10 will be examined on the merits.

***Claim Rejections - 35 USC § 102***

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 5-7, 9 and 10 are rejected under 35 U.S.C. 102(b) as being anticipated by Hidalgo et al. (Oncogene Vol. 19, pp.6680-6686, 2000).
5. The Claims are drawn to a method for determining the sensitivity of cancer in a subject to treatment with rapamycin or a rapamycin derivative, comprising determining the level of expression and phosphorylation state of S6 protein in a tumor sample from said subject.
6. Hidalgo et al. teach the use of rapamycin and rapamycin analog (CCI-779), which are both inhibitors of mTOR, as a treatment method for cancer therapy. Hidalgo et al. disclose "impressive antiproliferative activity has been demonstrated following

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treatment of diverse types of experimental tumors with rapamycin" (see p. 6680, right column, line 31-33). Rapamycin exerts concentration-dependent inhibition of cell proliferation and tumor growth in a variety of murine and human cancers growing in both cell culture and xenograft models including B16 melanoma, P388 leukemia, MiaPaCa-2 and Panc-1 human pancreatic carcinoma and tumors derived from B-cell lymphoma, small cell lung cancer carcinoma, and childhood rhabdomyosarcoma (see p. 6682, right column, 2<sup>nd</sup> paragraph). Hidalgo et al. also disclose that "rapamycin treatment results in a rapid and profound dephosphorylation of p70s6k (also known as S6) suppressing its activity (see p. 6682, left column, last sentence). The reference teaches each and every limitation of the claims.

### ***Claim Rejections - 35 USC § 103***

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

8. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

9. Claim 8 is rejected under 35 U.S.C. 103(a) as being unpatentable over Hidalgo et al. (Oncogene Vol. 19, pp.6680-6686, 2000) in view of Huang et al. (Curr. Opin. Investig. Drugs Vol.3(2), pp.295-304, 2002).

10. The Claim is drawn to a method for determining the sensitivity of cancer in a subject to treatment with the rapamycin derivative, 40-O-(2-hydroxyethyl) rapamycin, comprising determining the level of expression and phosphorylation state of S6 protein in a tumor sample from said subject.

11. The teachings of Hidalgo et al. are presented in the 102(b) rejection set forth above. Hidalgo et al. does not teach a method for determining the sensitivity of cancer in a subject to treatment with the rapamycin derivative, 40-O-(2-hydroxyethyl) rapamycin, comprising determining the level of expression and phosphorylation state of S6 protein in a tumor sample from said subject. This deficiency is made up for by Huang et al.

12. Huang et al. teach inhibitors of mammalian target of rapamycin as novel antitumor agents that are being developed as antitumor drugs and are undergoing clinical trials. Huang et al. teach two rapamycin derivatives, CCI-779 and RAD-001 (also known as SDZ-RAD and 40-O-(2-hydroxyethyl) as evidence by "Comparative Toxicogenomics Database"). Huang et al. discuss potential antitumor mechanisms and resistance mechanisms of mTOR inhibitors, and summarize the current status of CCI-779 and RAD-001 compounds as novel antitumor agents (see Abstract).

13. It would have *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to use the rapamycin derivative, 40-O-(2-hydroxyethyl)

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(RAD-001) in the method taught by Hidalgo et al. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by teachings in Hidalgo et al. and Huang et al. because Huang et al. teach that 40-O-(2-hydroxyethyl) is an mTOR inhibitor that potently suppress growth and proliferation of numerous tumor cell lines in culture or when grown in mice as xenografts.

### ***Conclusion***

14. Claims 5-10 are rejected.
15. No claim is allowed.
16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Meera Natarajan whose telephone number is 571-270-3058. The examiner can normally be reached on Monday-Thursday, 8:30AM-6:00PM, ALT. Friday. EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business

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Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

MN



LARRY R. HELMS, PH.D.  
SUPERVISORY PATENT EXAMINER